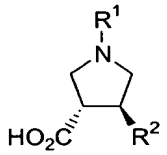
IN THE CLAIMS

A list of the currently pending claims as amended in the PCT Article 19 [35 USC 371(c)(3)] Amendment on November 10, 2004:

1. (original) A process for the preparation of compounds of structural formula (I):



(I)

wherein

R^1 is selected from the group consisting of

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) $-(CH_2)_n-C_{3-7}$ cycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl, and
(8) $-(CH_2)_n$-heteroaryl,

in which phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3; and alkyl, cycloalkyl, and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^2 is selected from the group consisting of

(1) C_{1-4} alkyl,
(2) $-(CH_2)_n$-cycloalkyl,
(3) $-(CH_2)_n$-heterocycloalkyl,
(4) $-(CH_2)_n$-phenyl,
(5) $-(CH_2)$n-naphthyl, and
(6) $-(CH_2)$n-heteroaryl wherein heteroaryl is selected from the group consisting of
    (1) pyridinyl,
    (2) furyl,
    (3) thienyl,

(4) pyrrolyl,
(5) oxazolyl,
(6) thiazolyl,
(7) imidazolyl,
(8) pyrazolyl,
(9) isoxazolyl,
(10) isothiazolyl,
(11) pyrimidinyl,
(12) pyrazinyl,
(13) pyridazinyl,
(14) quinolyl,
(15) isoquinolyl,
(16) benzimidazolyl,
(17) benzofuryl,
(18) benzothienyl,
(19) indolyl,
(20) benzthiazolyl, and
(21) benzoxazolyl;

in which alkyl, phenyl, naphthyl, heteroaryl, and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from R^3;

each R^3 is independently selected from the group consisting of

(1) C_{1-6} alkyl,
(2) $-(CH_2)_n$-phenyl,
(3) $-(CH_2)_n$-naphthyl,
(4) $-(CH_2)_n$-heteroaryl,
(5) $-(CH_2)_n$-heterocycloalkyl,
(6) $-(CH_2)_nC_{3-7}$ cycloalkyl,
(7) halogen,
(8) OR^4,
(9) $-(CH_2)_nN(R^4)_2$,
(10) NO_2,
(11) $-(CH_2)_nNR^4SO_2R^4$,
(12) $-(CH_2)_nSO_2N(R^4)_2$,
(13) $-(CH_2)_nS(O)_pR^4$,
(14) CF_3,

(15) CH_2CF_3,

(16) OCF_3, and

(17) OCH_2CF_3;

in which heteroaryl is as defined above; alkyl, phenyl, naphthyl, heteroaryl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy; and wherein any methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl; or two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group;

each R^4 is independently selected from the group consisting of

(1) hydrogen,

(2) C_{1-6} alkyl,

(3) $-(CH_2)_n$-phenyl,

(4) $-(CH_2)_n$-heteroaryl,

(5) $-(CH_2)_n$-naphthyl,

(6) $-(CH_2)_n$-heterocycloalkyl,

(7) $-(CH_2)_nC_{3-7}$ cycloalkyl, and

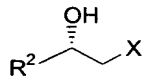
(8) $-(CH_2)_nC_{3-7}$ bicycloalkyl;

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy; or two R^4 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and NC_{1-4} alkyl; and

n is 0, 1, 2, 3 or 4;

comprising the steps of:

(a) preparing an alcohol of structural formula (V)

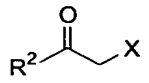


(V)

wherein

X is bromide or chloride, and R^2 is as defined above,

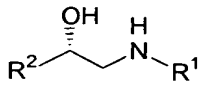
by treating a ketone of structural formula (IV),



(IV)

wherein X is bromide or chloride, and R^2 is as defined above, with a reducing agent, and isolating the resulting product;

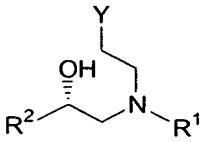
(b) forming an amino alcohol of structural formula (VII)



(VII)

wherein R^1 and R^2 are as defined above,
by treating the alcohol of structural formula (V) with an amine of general formula R^1NH_2, wherein R^1 is as defined above, and a base in a solvent, and isolating the resulting product;

(c) forming a compound of structural formula (VIII)



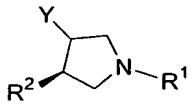
(VIII)

wherein Y is –CN or $-CO_2R^5$ and R^5 is C_{1-4} alkyl, and wherein R^1 and R^2 are as defined above, by treating the amino alcohol of structural formula (VII) with a compound of general formula (XI)

(XI),

wherein Y is –CN or $-CO_2R^5$, and R^5 is C_{1-4} alkyl, and isolating the resulting product;

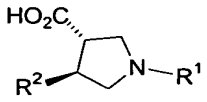
(d) forming a pyrrolidine compound of structural formula (X)



(X)

wherein Y, R^1 and R^2 are as defined above,
by treating the compound of structural formula (VIII) with an alcohol activating reagent, followed by a base;

(e) forming a trans-pyrrolidine acid of structural formula (I)



(I)

wherein R^1 and R^2 are as defined above,
by hydrolyzing the pyrrolidine compound of structural formula (X) with an aqueous base in a solvent; and

(f) isolating the resulting product.

2. (original) The process of Claim 1 wherein the reducing agent used to treat compound of formula (IV) of step (a) is (+)-DIP chloride.

3. (original) The process of Claim 1 wherein the compound of formula (IV) of step (a) is treated with a reducing agent selected from the group consisting of borane-N,N-diethyl aniline, borane-THF, and borane-dimethylsulfide, in the presence of a catalyst.

4. (original) The process of Claim 3 wherein the reducing agent is borane-N,N-diethyl aniline.

5. (original) The process of Claim 4 wherein the catalyst selected from the group consisting of (S)-CBS and (S)-2-methyl CBS oxazaborolidine.

6. (original) The process of Claim 5 wherein the catalyst is (S)-2-methyl CBS oxazaborolidine.

7. (original) The process of Claim 1 wherein the alcohol of formula (V) is treated with an amine of general formula R^1NH_2, wherein R^1 is selected from the group consisting of hydrogen, $-(CH_2)_n$phenyl, and C_{1-6}alkyl.

8. (original) The process of Claim 7 wherein R^1 is *tert*-butyl.

9. (original) The process of Claim 1 wherein the alcohol of formula (V) is treated with a base selected from the group consisting of NaOH, LiOH, and KOH.

10. (original) The process of Claim 9 wherein the base is NaOH.

11. (original) The process of Claim 1 wherein, the compound of formula (XI) is the compound wherein Y is –CN.

12. (original) The process of Claim 11 wherein the compound of formula (VIII) is formed by adding a 1:1 mixture of ethanol:formamide.

13. (original) The process of Claim 1 wherein the amino alcohol of formula (VIII) is treated with an alcohol activating reagent selected from the group consisting of $ClPO(OR^6)_2$, $ClPO(N(R^6)_2)_2$, MsCl, Ms_2O, TsCl, and Ts_2O, wherein R^6 is C_{1-4} alkyl or phenyl.

14. (original) The process of Claim 13 wherein the alcohol activating reagent is chlorodiethyl phosphate.

15. (original) The process of Claim 1 wherein amino alcohol of formula (VIII) is treated with a base selected from the group consisting of lithium hexamethyl disilazide, sodium hexamethyl disilazide, and potassium hexamethyldisilazide.

16. (original) The process of Claim 15 wherein the base is lithium hexamethyl disilazide.

17. (original) The process of Claim 1 wherein the pyrrolidine compound of formula (X) is hydrolyzed with a base selected from the group consisting of NaOH, LiOH and KOH.

18. (original) The process of Claim 17 wherein the base is NaOH.

19. (original) The process of Claim 1 wherein R^2 is phenyl or thienyl optionally substituted with one to three groups independently selected from R^3.

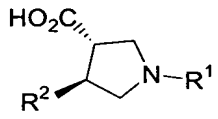
20. (original) The process of Claim 19 wherein R^2 is phenyl optionally substituted with one to three groups independently selected from R^3.

21. (original) The process of Claim 20 wherein R^3 is selected from the group consisting of halogen, $-CF_3$, and OR^4, wherein R^4 is as defined in Claim 1.

22. (original) The process of Claim 21 wherein R^2 is selected from the group of phenyl; *ortho, para*-difluorophenyl; and *para*-methoxyphenyl.

23. (original) The process of Claim 22 wherein R^2 is *ortho, para*-difluorophenyl.

24. (original) The process of Claim 1 wherein the compound of structural formula (I) is isolated by forming a zwitterion of the trans pyrrolidine acid of structural formula (I)



(I)

wherein R^1 and R^2 are as defined above; recrystallizing the zwitterion from a solvent; and isolating the resulting product.

25. (original) The process of Claim 24 wherein the zwitterion of the pyrrolidine acid of formula (I) is formed at the isoelectric pH using an acid.

26. (original) The process of Claim 25 wherein the acid is selected from sulfuric acid or hydrochloric acid.

27. (original) The process of Claim 26 wherein the acid is sulfuric acid.

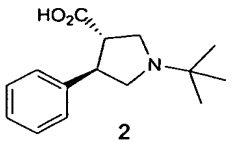
28. (original) The process of Claim 24 wherein the zwitterion of the pyrrolidine acid of formula (I) is recrystallized from a solvent.

29. (original) The process of Claim 28 wherein the solvent is selected from the group consisting of ethanol, isopropyl alcohol, methyl *tert*-butyl ether or a mixture thereof.

30. (original) The process of Claim 29 wherein the solvent is a mixture of 1:3 isopropyl alcohol:methyl *tert*-butyl ether.

31. (canceled in PCT Article 19 Amendment)

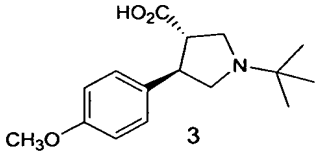
32. (original) The compound 2



2 ;

or a zwitterion or salt thereof.

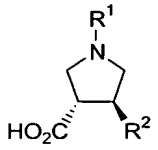
33. (original) The compound 3



3 ;

or a zwitterion or a salt thereof.

34. (original) A process for the preparation of compounds of structural formula (I):



(I)

wherein

R^1 is selected from the group consisting of

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) $-(CH_2)_n-C_{3-7}$ cycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl, and

(8) -$(CH_2)_n$-heteroaryl,

in which phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3; and alkyl, cycloalkyl, and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^2 is selected from the group consisting of

(1) C_{1-4} alkyl,

(2) –$(CH_2)_n$-cycloalkyl,

(3) –$(CH_2)_n$-heterocycloalkyl,

(4) –$(CH_2)_n$-phenyl,

(5) –(CH_2)n-naphthyl, and

(6) –(CH_2)n-heteroaryl wherein heteroaryl is selected from the group consisting of

(1) pyridinyl,

(2) furyl,

(3) thienyl,

(4) pyrrolyl,

(5) oxazolyl,

(6) thiazolyl,

(7) imidazolyl,

(8) pyrazolyl,

(9) isoxazolyl,

(10) isothiazolyl,

(11) pyrimidinyl,

(12) pyrazinyl,

(13) pyridazinyl,

(14) quinolyl,

(15) isoquinolyl,

(16) benzimidazolyl,

(17) benzofuryl,

(18) benzothienyl,

(19) indolyl,

(20) benzthiazolyl, and

(21) benzoxazolyl;

in which alkyl, phenyl, naphthyl, heteroaryl, and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from R^3;

each R^3 is independently selected from the group consisting of

(1) C_{1-6} alkyl,
(2) -$(CH_2)_n$-phenyl,
(3) -$(CH_2)_n$-naphthyl,
(4) -$(CH_2)_n$-heteroaryl,
(5) -$(CH_2)_n$-heterocycloalkyl,
(6) -$(CH_2)_n C_{3-7}$ cycloalkyl,
(7) halogen,
(8) OR^4,
(9) -$(CH_2)_n N(R^4)_2$,
(10) NO_2,
(11) -$(CH_2)_n NR^4 SO_2 R^4$,
(12) -$(CH_2)_n SO_2 N(R^4)_2$,
(13) -$(CH_2)_n S(O)_p R^4$,
(14) CF_3,
(15) CH_2CF_3,
(16) OCF_3, and
(17) OCH_2CF_3;

in which heteroaryl is as defined above; alkyl, phenyl, naphthyl, heteroaryl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy; and wherein any methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl; or two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group;

each R^4 is independently selected from the group consisting of

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) -$(CH_2)_n$-phenyl,
(4) -$(CH_2)_n$-heteroaryl,
(5) -$(CH_2)_n$-naphthyl,
(6) -$(CH_2)_n$-heterocycloalkyl,
(7) -$(CH_2)_n C_{3-7}$ cycloalkyl, and
(8) -$(CH_2)_n C_{3-7}$ bicycloalkyl;

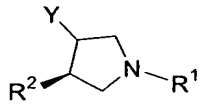
wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy;

or two R^4 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and NC_{1-4} alkyl; and

n is 0, 1, 2, 3 or 4;

comprising the steps of:

(a) hydrolyzing a pyrrolidine compound of structural formula (X), wherein Y is –CN or – CO_2R^5 and R^5 is C_{1-4} alkyl, and wherein R^1 and R^2 are as defined above,



(X)

with an aqueous base in a solvent; and

(b) isolating the resulting product.

35. (original) The process of Claim 34 wherein the pyrrolidine compound of formula (X) is hydrolyzed with a base selected from the group consisting of NaOH, LiOH and KOH.

36. (original) The process of Claim 35 wherein the base is aqueous NaOH.

37. (original) The process of Claim 36 wherein R^2 is selected from the group of phenyl; *ortho, para*-difluorophenyl; and *para*-methoxyphenyl.

38. (original) The process of Claim 37 wherein R^2 is *ortho, para*-difluorophenyl.

39. (original) The process of Claim 34 wherein R^1 is *tert*-butyl.